REMARKS

1. **Status of the Claims**

Claims 10 and 25 have been amended to more clearly present Applicants' invention. Support for these amendments can be found throughout the present specification, including in Example 2, at page 14, lines 5-8, which describes removal of samples from an aqueous solution without contamination from the contamination barrier. Therefore these amendments introduce no new matter.

Claims 10-17 and 24-29 are pending in the application, with claims 10 and 25 being the independent claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

The following remarks are submitted in response to the Office Action dated July 7, 2010, as well as the Advisory Action dated December 20, 2010.

2. **The Rejection of Claims 10-17 and 24 Under 35 U.S.C. § 103(a) Over Bloch in View of Rothmann Should be Withdrawn**

In the Office Action at pages 3-5, claims 10-17 and 24, have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Bloch *et al.*, U.S. Patent No. 5,411,876 in view of Rothmann *et al.*, Published U.S. Patent Application No. 2003/0065152 (hereinafter "Rothmann"). Applicants respectfully traverse this rejection.

The Office Action asserts that Bloch allegedly discloses a method for improving the processing of polymerase chain reaction (PCR) solution by adding mineral oil, waxes and greases to the surface as a barrier to both evaporation and contamination. However, the Office Action concedes that Bloch does not explicitly disclose that the contamination barrier prevents contamination during transfer of aqueous solutions and/or formation of aqueous aerosols, while also allowing for removal and processing of the aqueous solutions under the contamination barrier, or that the barrier comprises branched or unbranched hydrocarbons having 6 to 16 carbon atoms. *See* Office Action at page 4, second paragraph. The Office Action attempts to cure this deficiency with the disclosure of Rothmann.

The Office Action contends that Rothmann discloses a method that prevents contamination during the separation and purification of biopolymers, such as nucleic-acid containing polymers. The Office Action suggests that Rothmann discloses adding a layer of an immiscible hydrocarbon on top of an aqueous solution of the biopolymer, and that mineral oil is particularly preferred for this use.

The Office Action further contends that Rothmann discloses that hydrocarbons having 8 to 12 carbon atoms are suitable for this use. The Office Action concludes that it would have been obvious to modify the mineral oil barrier disclosed in Bloch and replace it with C_8 to C_{16} hydrocarbons as disclosed in Rothmann in order to prevent aerosol formation. Applicants respectfully disagree with these contentions and conclusions.

Applicants submit herewith a Declaration Under 37 C.F.R. § 1.132, of Dr. Thomas Rothmann ("the Rothmann declaration"), setting forth the distinctions between the presently claimed invention and the references cited in the Office Action.

Applicants submit that the obviousness rejection set forth in the Office Action is based on impermissible hindsight. *See* M.P.E.P. § 2145.X.A; *see also KSR Int'l. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1752 (2007). ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.") The Office Action has not set forth a proper *prima facie* case of obviousness. As set forth in M.P.E.P. § 2143(D), a *prima facie* case of obviousness can only be shown where the cited combination of references would yield predictable results. *See KSR*, 127 S.Ct. 1727 at 1740. The Office Action has not provided a showing that modifying the disclosure of Bloch with the disclosure of Rothmann would have a reasonable expectation of success --- i.e., a reasonable expectation that modifying the greases and waxes utilized in Bloch with the hydrocarbons disclosed in Rothmann, as required, would result in a successful method of preventing contamination. Absent such a showing, a *prima facie* case of obviousness cannot be established. *See* M.P.E.P. § 2143.02.

Applicants submit that the disclosure of Bloch relies on the use of greases or waxes to create a overlay on the surface of a PCR product. *See* Bloch at columns 3-4. The Office Action suggests that it would have been obvious to substitute hydrocarbons having 8 to 12 carbon atoms, as disclosed in Rothmann, for the greases and waxes utilized in Bloch. Applicants submit that, contrary to the assertions in the Office Action, Rothmann does not disclose "adding a layer of an immiscible hydrocarbon on top of an aqueous solution of the biopolymer." *See* Office Action at page 4, third paragraph. Instead, Rothmann discloses "the addition of branched or unbranched hydrocarbons to the aqueous mixtures which are to be analyzed and which contain the biopolymers or biopolymers as one component." Rothmann at page 2, paragraph 11. *See* the Rothmann declaration at pages 2-3, paragraph 8.

Applicants submit that "addition of branched or unbranched hydrocarbons" to the mixtures (i.e., *inclusion* in the aqueous solutions via *mixing*) as disclosed in Rothmann is not the same as *covering* the aqueous solution with a contamination barrier as required in the presently claimed

invention. (*See also* Rothmann at page 3, claim 1, "mixing an aqueous solution . . . with at least one hydrocarbon . . .) While Bloch may disclose the use of wax or grease overlays, there is no indication that the *addition* of branched or unbranched hydrocarbons to an aqueous mixture, as disclosed in Rothmann, would provide a sufficient "barrier against mixing of aqueous reagents segregated above and below the grease or wax layer," as in Bloch. *See* Bloch at column 4, lines 37-39. *See* the Rothmann declaration at page 3, paragraph 9.

There is no reasonable expectation that addition of branched or unbranched hydrocarbons to the solutions of Bloch would provide a sufficient barrier against mixing, which is a specific requirement of Bloch. The use of the branched or unbranched hydrocarbons in Rothmann to "allow elution to be carried out as completely as possible with reproducible elution volumes to avoid the contamination of other samples with fluids for analysis," provides no indication that these same hydrocarbons could function as barriers as required in Bloch. *See* the Rothmann declaration at page 3, paragraph 10. Applicants submit that such a modification would not yield predictable results, and thus, cannot support a *prima facie* case of obviousness. *See* M.P.E.P. § 2143.02. *See also KSR*, 127 S.Ct. at 1740.

Furthermore, Applicants submit that there would not have been a reasonable expectation of success that substituting the hydrocarbons disclosed in Rothman for the grease or wax overlay would produce a covering that *prevents contamination during transfer* of aqueous solutions, *and* the covering *prevents formation of aqueous aerosols*, while allowing for removal and processing of said aqueous solutions under the contamination barrier *without contamination from the contamination barrier*, as required in the presently claimed invention. *See* the Rothmann declaration at pages 3-4, paragraph 11.

The Advisory Action submits that "[r]eplacing oils, greases, and waxes with alkanes is nothing more than substituting one known prior art substance for another known prior art substance in the same application." Advisory Action at paragraph 1. In addition, the Advisory Action states "[t]he Examiner agrees that Bloch teaches some advantages of wax over oil, but those advantages are not associated with the function under consideration, i.e., preventing cross-contamination of DNA-containing samples during analysis."

Applicants respectfully disagree with this assertion and submit that the conclusions in the Advisory Action ignore the elements of the presently claimed invention that indicate that the claimed contamination barrier *prevents contamination during transfer* of aqueous solutions, *and prevents formation of aqueous aerosols*, while allowing for removal and processing of said aqueous solutions *without contamination from the contamination barrier*. Applicants submit that the Advisory Action

ignores the disclosure of Bloch that clearly teaches away from the use of liquid-phase oil overlays to achieve these goals, and instead directs one of ordinary skill in the art toward the use of solid-phase greases or waxes. *See* the Rothmann declaration at page 4, paragraph 12.

As disclosed in Bloch, "[t]he mineral oil overlay introduces several practical problems: (a) mineral oil contamination of reaction mixture samples withdrawn for post-PCR analysis." Bloch at column 3, lines 41-44. Thus, Bloch clearly indicates that mineral oil overlays are not desirable as contamination barriers as these oils cause contamination of samples withdrawn for post-PCR analysis, i.e., they are not desirable for removal and processing of PCR solutions without contamination from the contamination barrier, as in the presently claimed invention. Rather, Bloch directs one of ordinary skill in the art to "replace the mineral oil overlay with a layer of grease or wax, the solidity of which at room temperature or below creates a barrier." Bloch at column 4, lines 35-40. Bloch further states that "wax, unlike oil, does not cling to the piper [sic] used to withdraw PCR product after amplification and, therefore, does not contaminate post PCR-detection reactions." Bloch at column 8, lines 25-31. *See* the Rothmann declaration at page 4, paragraph 13.

Therefore, Applicants respectfully submit that there would not have been a reasonable expectation of success that substitution of a liquid-phase hydrocarbon (i.e., hydrocarbons of from 6 to 16 carbon atoms as utilized in the presently claimed invention) for the solid-phase waxes and greases disclosed in Bloch would not only *prevent contamination during transfer* of aqueous solutions, *and prevent formation of aqueous aerosols*, but also allow for removal and processing of said aqueous solutions *without contamination from the contamination barrier*. Thus, a *prima facie* case has not been established. *See* the Rothmann declaration at page 5, paragraph 14.

In addition, as set forth in the Rothmann declaration at page 5, paragraph, 6 it is a surprising and unexpected result of the presently claimed invention that a contamination barrier comprising at least one water immiscible hydrocarbon or hydrocarbon mixture comprosing branched or unbranched hydrocarbons of from 6 to 16 carbon atoms would prevent contamination during transfer of aqueous solutions, and also prevent formation of aqueous aerosols, while allowing for removal and processing of the aqueous solutions under the contamination barrier without contamination from the contamination barrier.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

3. The Rejection of Claim 25 Under 35 U.S.C. § 103(a) Over Bloch in View of Kosak Should be Withdrawn

In the Office Action at pages 5-6, claim 25 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Bloch in view of Kosak *et al.*, U.S. Patent No. 5,968,729 (hereinafter "Kosak"). Applicants respectfully traverse this rejection.

The Office Action suggests that Bloch discloses the claimed invention as set forth above, but indicates that Bloch does not disclose that the contamination barrier comprises silicone oil. The Office Action attempts to cure this deficiency with Kosak.

The Office Action contends that Kosak discloses a method to seal an aqueous PCR tube with a grease or wax layer, and that acceptable greases must be inert and immiscible with water, such as silicone grease. The Office Action states:

> Kosak does not disclose silicone oils for use as barriers on aqueous PCR solutions. However, Bloch teaches that oils, greases, and waxes are all suitable for use as barriers on aqueous PCR solutions, as discussed above. Therefore it is considered *prima facie* obvious that silicone greases and silicone oils are both suitable for use as such barriers.

Office Action at page 6, second paragraph. Applicants respectfully disagree with these contentions and conclusions.

As an initial matter, Applicants respectfully disagree with the assertion in the Office Action that "Bloch teaches that oils, greases, and waxes are all suitable for use as barriers on aqueous PCR solutions." While Bloch may indicate that mineral oil is commonly used as a vapor barrier to minimize solvent evaporation (*see* Abstract), it clearly indicates problems associated with the use of oil as a contamination barrier as in the presently claimed invention. In fact, Bloch specifically points out a number of reasons that oil is not an appropriate contamination barrier for preventing contamination during transfer of aqueous solutions and formation of aqueous aerosols, while also allowing removal and processing of these solutions without contamination from the contamination barrier. *See* Bloch at column 3, lines 41-52.

Bloch clearly teaches away from the use of liquid-phase oils, and specifically focuses on replacement of mineral oil "with a layer of grease or wax, the solidity of which at room temperature of below creates a barrier against mixing of aqueous reagents." *See* Bloch at column 4, lines 36-40. Kosak also teaches away from the use of liquid oils, stating that "[t]he preferred sealer is a *solid material*, such as wax, grease or polymer mix, that *does not easily flow when solidified at room temperature* (i.e. 25°C.)." Kosak at column 5, line 66, through column 6, line 67 (emphasis added).

Applicants submit that as both Bloch and Kosak specifically teach away from the use of liquid oils as contamination barriers, a person of ordinary skill in the art would clearly not have considered it obvious to utilize any oil, let alone silicone oils, in either of the methods of Bloch or Kosak.

Thus, contrary to the assertion in the Office Action, present claim 25, which specifically requires the use of a liquid, silicone oil, would not have been obvious based on the disclosure of the cited references, alone or in combination. In fact, the suggestion in the Office Action that "it would have been *prima facie* obvious to one of ordinary skill in the art to modify the mineral oil barrier of Bloch and utilize a silicone barrier as taught by Kosak because it is easier to penetrate an oil layer than a grease layer," (Office Action at page 6, third paragraph) specifically goes *against* the disclosure of both Bloch and Kosak which repeatedly specify the use of a grease or wax layer that is *solid* at room temperature.

As discussed above, applications respectfully disagree with the statement in the Advisory Action that "[t]he Examiner agrees that Bloch teaches some advantages of wax over oil, but those advantages are not associated with the function under consideration, i.e., preventing cross-contamination of DNA-containing samples during analysis." As set forth above, the presently claimed invention indicates that the claimed contamination barrier *prevents contamination during transfer* of aqueous solutions, *and prevents formation of aqueous aerosols*, while allowing for removal and processing of said aqueous solutions *without contamination from the contamination barrier*. Applicants submit that the Advisory Action ignores the disclosure of Bloch that clearly teaches away from the use of liquid-phase oil overlays, including silicone oil, to achieve these goals, and instead directs one of ordinary skill in the art toward the use of solid-phase greases or waxes. *See* the Rothmann declaration at page 4, paragraph 12.

Therefore, Applicants respectfully submit that there would not have been a reasonable expectation of success that substitution of a silicone oil for the solid-phase waxes and greases disclosed in Bloch would not only *prevent contamination during transfer* of aqueous solutions, *and prevent formation of aqueous aerosols*, but also allow for removal and processing of said aqueous solutions *without contamination from the contamination barrier*. Thus, a *prima facie* case has not been established.

In view of the foregoing remarks, Applicants respectfully submit that the Office Action has not set forth a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are therefore respectfully requested.

4. The Rejection of Claims 26-29 Under 35 U.S.C. § 103(a) Over Bloch in View of Kosak and Moretto Should be Withdrawn

In the Office Action at pages 6-8, claims 26-29 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Bloch in view of Kosak and further in view of Moretto *et al.*, "Silicones" in Ullmann's Encyclopedia of Chemical Technology (hereinafter "Moretto"). Applicants respectfully traverse this rejection.

The Office Action suggests that Bloch in view of Kosak discloses the claimed invention as set forth above. The Office Action concedes, however, that the combination of references does not explicitly disclose silicone oils that are comprised of unbranched chains of silicon and oxygen atoms having 10 to 1000 silicon atoms.

The Office Action attempts to cure this deficiency with the disclosure of Moretto, suggesting that Moretto discloses that the most important silicone fluids are methyl silicone fluids comprised of unbranched chains containing silicon and oxygen atoms. The Office Action concludes that "it would have been *prima facie* obvious to one of ordinary skill in the art to modify the silicone oil barrier as taught by Bloch, in view of Kosak, with unbranched silicones containing 10 to 1000 silicon atoms because these silicones are the most important silicone fluids and are readily available." Office Action at page 7, third paragraph. Applicants respectfully disagree with these contentions and conclusions.

As set forth above, Applicants submit that both Bloch and Kosak specifically *teach away* from the use of liquid-phase oils as contamination barriers. While the Office Action contends that these references in combination disclose "a silicone oil barrier," both references specifically discuss the pitfalls of utilizing an oil layer as a contamination barrier and specifically require the use of waxes and oils that are *solid* a room temperature. *See* e.g., Bloch at column 4, lines 33-40; Kosak at column 5, line 66, through column 6, line 2. Thus, even if Moretto does disclose that the most important silicone fluids are methyl silicone fluids comprised of unbranched chains containing silicon and oxygen atoms, such a disclosure, in combination with the disclosures of Bloch and Kosak, does not render obvious the presently claimed invention. The Office Action has not provided a showing that modifying the disclosures of Bloch and Kosak with the disclosure of Moretto would have a reasonable expectation of success of creating a contamination barrier, as presently claimed. Absent such a showing, a *prima facie* case of obviousness cannot be established. *See* M.P.E.P. § 2143.02.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

Applicants believe that the claims are in condition for allowance and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful in resolving any issues.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-5071.

Respectfully submitted,

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